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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,536	03/03/2004	Lin Shiue Lian	8961-000010/US	3361

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EXAMINER

BERTOGLIO, VALARIE E

ART UNIT PAPER NUMBER

1632

DATE MAILED: 07/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/791,536	LIAN ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03/03/04 and 07/02/04 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>03/03/04</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims 1-24 are pending and under consideration in the instant office action.

Claim Objections

Claim 1 is objected to because of the following informalities: Step (c) of claim 1 is awkward as written. While it is clear that the step is intended to require screening the new transgenic progeny for phenotypes or patterns that are different from the parent fish, as written it appears that fish with different phenotype or pattern are screened for some unrecited characteristic. Appropriate correction is required.

Claims 8 and 9 are objected to because of the following informalities: The phrase "body transparent levels" at line 2 of each claim is awkward as written. The term "transparency" would more clearly indicate what appears to be intended. Appropriate correction is required.

Claim 20 is objected to because of the following informalities: The claim ends with improper punctuation. Appropriate correction is required.

Claim 21 is objected to because of the following informalities: The claim is grammatically improper with the phrase "new transgenic progenies is". Appropriate correction is required.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for generating an ornamental fish comprising steps of (a) generating a transgenic oviparous teleost fish whose genome comprises one or more genes encoding a fluorescent protein, operably linked to a promoter wherein the transgene is expressed in the fish; (b) breeding the transgenic fish with a fish of the same or different species having a phenotype or pattern that differs from the transgenic fish; and (c) screening the resulting transgenic progeny for those showing a phenotype or pattern that differs from each parent and fish made by the method, does not reasonably provide enablement for the claimed method with a transgenic viviparous fish, a transiently transfected transgenic fish comprising the transgene extrachromosomally or a transgenic fish wherein the transgene is not expressed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of

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experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

In general, the specification teaches making transgenic fish expressing a transgene encoding a fluorescent protein by microinjection of DNA into a 1-celled embryo using fish species that lay eggs that are fertilized and develop outside of the mother. The specification teaches operably linking the fluorescent protein-encoding genes to promoters that result in expression of the fluorescent protein in various patterns. The specification teaches mating, or crossing by in vitro fertilization, the transgenic fish to fish of the same or different species with different morphological traits or pigment patterns to ultimately create novel phenotypes wherein the resultant fish exhibits a phenotype that differs from either parent.

More specifically, the specification teaches use of closely related Danio and Medaka species of fish. Both are teleost species that lay unfertilized eggs, can be made transgenic and are amenable to in vitro fertilization and development. The specification fails to teach applying transgenic technology to non-teleost fishes or in carrying out the claimed method using live bearing (viviparous) fish either in transgenesis or in mating to transgenic oviparous teleost fishes.

With respect to generating transgenic fish of any species, the specification is not enabling for all fish species, including non-teleost and live-bearing species. The specification teaches making transgenic teleost zebrafish and medaka species and prophetically teaches using the claimed transgenic methods for other fish species. The specification teaches microinjection of

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DNA into the yolk, upon which cells divide to form a syncytium (page 6, paragraph 2; page 12, paragraph 2). The DNA can diffuse into the overlying cells during the first cell divisions, a property common to teleost fishes. The specification defines the claimed methods as being applicable to any species of fish (page 4, paragraph 2). However, the specification fails to define any parameters as guidance as to what fish species are amenable to transgenesis. As such, the claims encompass any fish species, of which live-bearing fish are not enabled by the specification. One of skill in the art would not know how to culture an egg of a live bearing fish, introduce a transgene and place it back into a female host to complete embryonic development. Neither the specification nor the art of record teaches how to make transgenic any species of fish wherein the fish are born live and eggs and embryos develop internally inside female fish as encompassed by the claims.

Furthermore, the art at the time of filing also taught that heterospecific insemination is a characteristic specific to teleost fishes as a result of the absence of an acrosome on sperm [Pandian and Kirankumar, **Current Science**, 85:917-931, specifically page 921, col. 2, paragraph 2]. Because the specification and the art of record is limited transgenesis in teleost fishes and heterospecific insemination is limited to teleost fishes, the claimed method can only be carried out using teleost species. Therefore, claims should be limited in scope to transgenic oviparous teleost species of fish where the egg structure is similar to that exemplified in the instant specification, is amenable to transgenesis and the embryo develops externally.

The claims encompass use of transgenic fish wherein the transgene is maintained episomally or extrachromosomally and is not integrated into the genome of the transgenic fish.

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The claimed method, however, requires that the transgene be heritable in order for the hybrid progeny to possess the transgene and express the desired trait. Therefore, the claims should require that the transgene be integrated into the genome and thereby be heritable. Use of terminology such as "...a transgenic fish whose genome comprises one or more genes..." would overcome this aspect of the rejection.

The claims also fail to require that the transgene of the transgenic fish be operably linked to a promoter and be expressed. The specification teaches use of fish promoters to drive expression of fluorescent protein encoding genes. The specification does not teach use of fluorescent protein encoding genes that are not operably linked to a promoter. Without promoter sequences, a transgene will not be expressed in the resulting fish. The specification also fails to teach how to carry out the claimed method wherein the transgene is not expressed. Claims should be amended to require that the gene encoding a fluorescent protein be operably linked to a promoter and that the fluorescent protein be expressed.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites the limitation "the fish" in line 1. There is insufficient antecedent basis for this limitation in the claim. It is unclear which fish, of the two fish recited in claim 1, is being referred to. Claims 12-19 depend from claim 11.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,2,8,9 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Lawson and Weinstein [**Developmental Biology**, 248:307-318].

Claims 1 and 2 are drawn to a method of making a fish comprising steps of generating a transgenic fish, breeding said fish to a second fish that has a different phenotype or pattern and screening the transgenic progenies for those exhibiting a phenotype or pattern that differs from the parents. Claims 8 and 9 limit the phenotype to certain observable morphological phenotypes including body transparent levels. Claim 23 is limited to the fish made by the method of claim 1.

Lawson and Weinstein taught generating a transgenic GFP expressing zebrafish using wild-type, pigmented (EK; page 310, col. 1, paragraph 3) *Danio rerio* (*Brachydanio rerio*). The transgenic fish was mated to an unpigmented albino mutant of the same species, resulting in a transgenic GFP, albino mutant. For example, see Figure 5 and legend. Albino mutants have an altered body transparent level as a result of a loss of pigmentation.

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Thus, Lawson and Weinstein taught all of the limitations of claims 1,2,8,9 and 23.

Double Patenting

Applicant is advised that should claim 1 be found allowable, claim 2 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725.

The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Valarie Bertoglio
Examiner
Art Unit 1632